2

(19)日本国特許庁（ＪＰ）　(12)公開特許公報（Ａ）　(11)特許出願公開番号

特開平8－183737

(43)公開日　平成8年(1996)7月16日

(51)Int.Cl.[6]	識別記号	庁内整理番号	ＰＩ	技術表示箇所
Ａ６１Ｋ　31/70				
// Ｃ０７Ｈ　19/16				

審査請求　未請求　請求項の数2　ＦＤ　（全４頁）

(21)出願番号　特願平6－337674

(22)出願日　平成6年(1994)12月28日

(71)出願人　000126757
株式会社アドバンス
京京都中央区日本橋小舟町５番７号

(72)発明者　下橋　博隆
京京都小平市小川町１丁目877番地

(72)発明者　難波　希三子
京京都新宿区中落合４丁目８番地５号

(72)発明者　岡部　敬一郎
京京都世田谷区成城８丁目30番地28号

(54)【発明の名称】　アルコール吸収抑制剤

(57)【要約】
【目的】体内でのアルコール吸収を抑制させ、アルコール摂取を自然に控えさせるような組成物を提供する。
【構成】メチルチオアデノシン（5'-デオキシ-5'-メチルチオアデノシン、ＭＴＡ）、その類似体、その誘導体のいずれか１つ乃至複数を含有する。

PATENT ABSTRACTS OF JAPAN

(11)Publication number : **08-183737**
(43)Date of publication of application : **16.07.1996**

(51)Int.CI. **A61K 31/70**
// C07H 19/16

(21)Application number : **06-337674**
(22)Date of filing : **28.12.1994**

(71)Applicant : **ADVANCE CO LTD**
(72)Inventor : **SHIMOHASHI HIROTAKA**
NANBA KIMIKO
OKABE KEIICHIRO

(54) ALCOHOL ABSORPTION INHIBITOR

(57)Abstract:
PURPOSE: To provide an alcohol absorption inhibitory composition which suppress the absorption of alcohol in vivo and naturally allow a person to decrease alcohol intake.
CONSTITUTION: This alcohol absorption inhibitor comprises at least one of methyladenosine (5'-deoxy-5'-methylthioadenosine, MTA), its analog, and their derivatives. As this component, are cited adenosine, an analog; 5'-deoxy-5'- chloroadenosine, N-6-methyl-adenosine, N-6-benzyladenosine, 2-chloroadenosine, 5'-deoxyisobutylthioadenosine, spongoadenosine and S-adenosylmethionine which is readily decomposed into MTA. MTA is given before or when one drinks alcohol, to inhibit alcohol from being absorbed whereby drunkenness is reduced the accumulation in the stomach is increased to reduce the amount of the alcohol to be drunk.

LEGAL STATUS

[Date of request for examination]

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision of rejection]

[Date of requesting appeal against examiner's decision of rejection]

[Date of extinction of right]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] this invention prevents acute **** by large ** of the ardent spirits (alcoholic beverage), and acute-alcoholism sideration, or relates to the constituent as the new functional foods which can expect the polyposia prevention effect and a polyphagia depressor effect, and an alcoholic absorption inhibitor.
[0002]
[Description of the Prior Art] Drink of moderate alcohol improves the circulation and is useful to the health of mind and body by being useful to a dissolution of stress. on the other hand, the polyposia of alcohol not only causes digestive trouble, but the long polyposia across which it boils and goes produces a fatty liver and critical illnesses, such as liver cirrhosis, further Moreover, it also becomes a social problem while it has influence with alcoholism (dependence) serious for the domestic financial side in nervus. Moreover, acute ****, acute-alcoholism sideration, etc. in alcoholic uptake are a troublesome problem socially. By the way, although it was known until now that an acetic acid, a citric acid, etc. will suppress absorption of alcohol as the bile and organic acid of a cow (****** et al. : alcoholic metabolism and liver 7, 75- 84, 1988), those alcoholic depressor effects were not things to the extent that it is so much expectable. Moreover, although there is a disulfiram which suppresses aldehyde dehydrogenation activity as disagreeable wine, the clinical symptom accompanied by pain is known very much.
[0003]
[Problem(s) to be Solved by the Invention] In order to carry out the prevention resolution of such a problem, this invention suppressed the absorption in the body of alcohol, and it made into the technical probrem to offer the constituent which can cut down alcoholic intake very automatically further.
[0004]
[Means for Solving the Problem] In order to solve this technical probrem, it devised zealously and resulted in the following invention. That is, artificers are the methylthio adenosines which were observing the physiological activity previously. (MTA) Although it is little it contains in the organization of almost all animals and plants -- having -- **** -- one sort Enterococcus faecium of a lactic-acid-bacteria group **** -- extracted MTA An antibacterial effect is in **** considered to be the cause bacillus of gum disease. moreover, it extracted from yeast in large quantities MTA It is further MTA although it had found out having a curative effect to the acute gastric ulcer of a rat (bottom bridges : application pharmacology 47, 91- 97, 1994). In the process in which medicinal action is investigated Absorption from the gastrointestinal tract of alcohol which carried out internal use to the rat MTA It found out suppressing. MTA Molecular weight 293.7 and the melting point It is the white powder of 228 - 230 ** , and in ordinary temperature, although it is refractory to distilled water, in warm water or acid water, it solves well. There is the characteristic feature which hardly melts also into ethyl alcohol or an acetone.
[0005] The alcoholic absorption inhibitor of this invention can also be used by the matter independent, and can also be added and used for a usual extensive ingesta. the amount used about 1-40mg/kg -- just before alcoholic drink or a meal -- or it is used simultaneously the matter which has these effects ****** -- the adenosines including a methylthio adenosine (MTA), and the derivative of those ****** 5' -- a - deoxy-5'- ****** adenosine, N-6-methyl adenosine, N-6-benzyl adenosine, 2-****** adenosine, and 5'-deoxy isobutyl thio adenosine and ****** gore denosin (adenosine-9beta-D-arabino furanoside) -- it decomposes easily -- having -- MTA It becomes. S adenosylmethionine can illustrate.
[0006]
[Effect of the Invention] Since the stay term in the stomach becomes long while MTA is mitigated and drunkenness is made to mitigate by the absorption suppression from the stomach and the intestine of alcohol drinking before or by taking simultaneously, the amount of stores can increase, and the amount of alcohol which a feeling of fullness becomes easy to produce easily, and is drunk can also be lessened. Moreover, MTA 1 time of the amount of take of meals comes to decrease, and it is effective also in the diet.
[0007] It is an animal experiment and the ground is MTA. It is based on the blood drug concentration of the alcohol given by recipe having fallen. moreover -- MTA A stomach contents is based on the fact of delaying time discharging to a duodenum. That is, the residence time in the stomach of the eaten object is lengthened.
[0008]
[Example] While the example of an experiment is shown MTA Ethanol absorption depressant action is explained.
[Example-of experiment1] MTA Ethanol absorption depressant action was examined using the rat (Wistar system, a male, weight 230-266g). MTA 0.2% The specific-salt liquid (CMC) of a carboxymethyl cellulose was made to suspend (it melts in part). To

the rat which carried out 1 night fast (one groups [five]) MTA 3.5 mg/kg, 10 mg/kg, and 30 mg/5 ml/kg Internal use is carried out and it is CMC in a control group. Liquid (1 / 200 capacity of weight) was prescribed for the patient. After 30 minutes 20% It is weight about ethyl alcohol. 1/200 Capacity internal use is carried out and it is 0.5, 1, 2, 3, and 4. It collected blood from the tail vena or the eye-socket venous plexus after time. Ethanol in a blood serum 6% CuSO4 and 5H2O (V/V) 1.25% NaOH (W/V) After carrying out a deproteinization, respectively in addition to a blood serum equivalent [every], determination was carried out with the gas chromatography (Hitachi-163). The condition is as follows. Detection law;FID, column;GASKUROPACK 54, mesh 80/100, and phi3x200mm (chromatography research stock), Column temperature;200 degree C, injection temperature;200 degree C, N2 flow;1.5 kg/cm2, H2flow; 1.0 kg/cm2 and Air flow; 0.8 kg/cm2. The alcoholic value in a blood serum A mean ** standard error (mg/dl) It was come out and expressed. Statistical processing of a between groups Student Under [all / it carries out by t-certification and / 0.05 / P< / or less / significant difference] (*P<0.05 and **P<0.01).

[0009] [result-1] result Table-1 the ethanol by which internal use was carried out by the control group is quickly absorbed from a gastrointestinal tract so that it may be shown -- having -- 30 a part -- after -- the blood serum alcoholic value turned into maximum (83.4**9 mg/dl) And 4 hours after, it became the minute amount. MTA 10 mg/kg and a 30 mg/kg medication group -- the amount of blood serum alcohol by after [ethanol medication] 1 hour or, 2 hours -- remarkable -- decreasing -- MTA each dose -- the maximum of alcohol -- blood serum of 1 hour 57.1**2.4 mg/dl 44.5**2.6 mg/dl it was . MTA 3.5 mg/kg The inclination that a medication group, on the whole, also reduces blood serum alcoholic concentration was shown.

[Table 1]

ＭＴＡのエタノール吸収抑制作用
(20% エチルアルコールを体重の 1/200 容量経口投与)

ＭＴＡ投与量 mg/kg	血清のアルコール濃度(mg/dl) 0.5 h	1 h	2 h	3 h	4 h
対照(0.2% CMC)	83.4±9.0	68.5±3.7	40.9±8.9	18.2±8.9	6.9±2.3
ＭＴＡ 3.5	70.3±3.0	67.9±2.0	31.8±1.5	5.7±0.5	3.8±0.3
10	55.7±4.3*	57.1±2.4*	27.5±2.7	6.2±0.2	7.1±0.5
30	35.5±2.3**	44.5±2.6**	14.6±2.7*	7.1±0.9	7.3±0.8

[0010] Next, ******** medication is carried out. 20% While the amount of ethanol is doubled [about] (1 capacity for of weight 100) and the blood serum alcoholic value is measured with time, the amount of alcohol which remains in the stomach 3 hours after is measured. MTA The effect of recipe was examined.

[0011] The [example-of experiment 2] rat (Wistar system, a male, weight 260-300 g) was used by one groups [four]. To the rat which carried out 1 night fast 0.2% CMC It prepared with liquid. MTA 0, 10, and 40 mg/5 ml/kg Internal use is carried out (1 / 200 capacity of weight), and it is 30. Later 20% It is weight about ethyl alcohol. Internal use of the 1/100 amount was carried out. And 0.5, 1, 2, and 3 It collected blood after time and the blood serum was obtained. The esophagus near a stomach cardia and the duodenum origin section were litigated from the rat of 3 hours which carried out the immediately after [blood collecting] bleeding fatality, the stomach was extracted, and the stomach weight was measured. Moreover, the stomach contents was taken out and capacity and the amount of alcohol were measured about the centrifugal (3000rpm and 15 min) supernatant liquid. With the gas chromatography, since the determination of alcohol required time, it was performed by the enzymatic process (Beutler and O.H.(1984) Methods of enzymatic analysis (Ed.by Bergmeyer H.U.6,598-613 and Verlag Chemie Weinheim).). The method of presentation of the concentration of the alcohol for every rat group and statistical processing of a between groups are statistical processing in part, although it is the same as that of [experiment-1]. Mann-Whitney U-test It was used. [0012] [Result-2] The result was shown in table-2. control group 0.5 although the blood serum alcoholic concentration after time showed maximum (121.3**6.0 mg/dl) -- MTA 10 mg and 40 mg/kg a medication group -- the blood serum of 1 hour after -- alcoholic concentration -- the maximum -- becoming -- respectively -- 79.5**6.1 mg/dl and 36.0**12.0 mg/dl It is a low value clearly and having suppressed absorption of the alcohol from a gastrointestinal tract was shown. Moreover, MTA 10 mg/kg By the medication group 0.5 Time A significant fall is statistically looked at by the blood serum alcoholic concentration of 1 hour, and it is at an MTA 40 mg/kg medication group. 0.5 From time 3 The significant fall of alcoholic concentration was accepted by the whole serum to time.

[Table 2]

ＭＴＡ のエタノール吸収抑制作用
(20% エチルアルコールを体重の 1/100 容量経口投与)

ＭＴＡ投与量 mg/kg	血清アルコール濃度 (mg/dl) 0.5 h	1 h	2 h	3 h
対照(0.2% CMC)	121.3±6.0	112.5±4.6	69.6±2.9	21.5±0.9
ＭＴＡ 10	78.0±14.0*	79.5±6.1**	56.5±4.7	23.6±5.6
40	33.4±7.1**	36.0±9.9**	23.1±6.1**	6.4±4.0**

[0013] The stomach was extracted from the rat which collects blood and carried out the bleeding fatality at the time of an end of [experiment-3] above-mentioned experiment-2 (with i.e., 3 hours after alcoholic medication), and the amount of residual alcohol in the stomach was measured to the stomach weight containing a contents, the amount of gastric juices, and the pan.

[0014] The stomach weight containing [result-3] contents, and MTA It became large in dose dependence and the content volume of the stomach also increased. Furthermore, it is MTA although the residual [in the stomach] total amount of alcohol was also a minute amount very much in the control group. By the medication group, it increased in dose dependence. Namely, MTA A

stomach contents suggests delaying time moving to below a duodenum from the stomach.

[Table 3]

ＭＴＡ投与の胃重量、胃液量、胃内残存アルコール量への影響
（20% エチルアルコールを体重の 1/100 容量経口投与）

ＭＴＡ投与量 (mg/kg)	胃重量 (g)	胃液量 (ml)	総アルコール量@ (mg)
対照(0.2% CMC)	1.73±0.04	0.05±0.02	0.01±0.01
ＭＴＡ 10	2.23±0.11**	0.15±0.79*	0.39±0.16*
40	3.07±0.26**	0.60±0.11**	17.89±5.55*

@ : Mann-Whitney の U-test

[0015] To the mouse (ICR system, a male, weight 30-36 g) of one groups [five] which carried out the [experiment-4] 1 night fast, it is CMC 0.2%. It prepared. MTA 3, 10, 40, and 160 mg/10 ml/kg Internal use (1/100 capacity of weight) was carried out. 30 It is Evans-Blue foods (Evans Blue is melted in 0.5% CMC liquid so that it may become 0.3%) 0.25 ml after a part. Internal use was carried out. and -- 30 a part -- after -- it slaughtered by cervical vertebrae luxation and asked for the proportion (%) of the travel of the coloring matter foods to a small-intestine overall length In addition, the stomach of the mouse which the inside of the stomach of the mouse made to abstain from food on a ****** chip is filled with a chip, and was made to abstain from food on a wire gauze was ****. It expresses with a mean ** standard error, and the numeric value for every group is in a significant difference detection of a between groups. Student t-certification is used. $P< 0.05$ The following was made significant.

[0016] [Result-4] MTA The operation to gastrointestinal-tract movement was shown in Table 4.

[Table 4]

ＭＴＡの小腸輸送能に対する作用

ＭＴＡ投与量 mg/kg	色素食輸送能 (%) 空 胃	充満胃
対照(0.2% CMC)	69.3±1.1	65.0±2.3
ＭＴＡ 3	64.2±4.9	60.2±4.7
10	60.6±5.0	51.8±6.5
40	54.5±2.0**	17.4±6.4**
160	40.8±1.2**	0 ±0**

Rate of flow in a small intestine of the Evans-Blue foods (coloring matter foods) prescribed for the patient into the stomach MTA 3 mg and 10 mg/kg Although the fall inclination was seen [group / medication / a control group], the statistical significant difference did not accept. By MTA 40 mg and the 160 mg/kg medication group, as for transportation ability, the mouse with **** and the fullness stomach (stomach full of a floor-cloth chip) fell clearly. And although coloring matter foods were moving all examples into the small intestine from the stomach with the mouse of ****, it is with the mouse of the fullness stomach. By three animals, coloring matter foods could not be found [an MTA 40 mg/kg medication group / a 160 mg/kg medication group] out in the small intestine in the example of all [in five animals] among five animals, but it had stopped in the stomach. That is, the exocytosis of the contents to a small intestine is received from the stomach. MTA It is more remarkable than the time of the way when the object eaten in the stomach is contained being ****, and a depressor effect is MTA. It became clear to have in the stomach the operation which stops food for a long time.

[Translation done.]